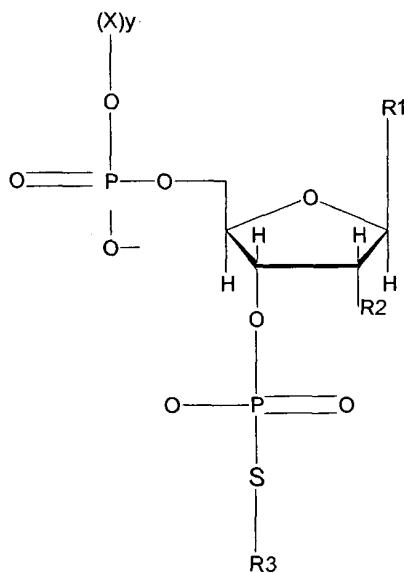


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CURRENT STATUS OF ALL CLAIMS

1. (Original) A method of non-enzymatic ligation of a nucleic acid, comprising contacting a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide under conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide.

2. (Amended) The method of claim 1, wherein said polynucleotide-3' phosphorothiolate ~~further comprises a 3'-SNP moiety~~ comprises a moiety having the formula:



wherein,

X is a nucleotide;

y is a positive integer;

R1 is a nucleotide base;

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R2 is a hydrogen atom or hydroxyl; and  
R3 is nitrophenyl.

3. (Original) The method of claim 1, wherein said polynucleotide-3' phosphorothiolate further comprises a duplex polynucleotide.

4. (Original) The method of claim 1, wherein said acceptor polynucleotide further comprises a duplex polynucleotide.

5. (Amended) ~~The method of claim 1, further comprising~~ A method of generating a polynucleotide product, comprising:

(a) contacting a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide under conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide, wherein a polynucleotide-3' phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide is formed, and

(b) transducing into a host cell a said polynucleotide-3' phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide.

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6. (Amended) ~~The method of claim 1, further comprising the step:~~ A method of non-enzymatic ligation of a nucleic acid, comprising:

(a) contacting a polynucleotide-3' phosphorothiolate precursor and an activator under conditions sufficient to react said polynucleotide-3' phosphorothiolate precursor and said activator to produce said a polynucleotide-3' phosphorothiolate, and

(b) contacting said polynucleotide-3' phosphorothiolate with an acceptor polynucleotide under conditions that allow formation of a phosphodiester bond between said polynucleotide-3' phosphorothiolate and said acceptor polynucleotide.

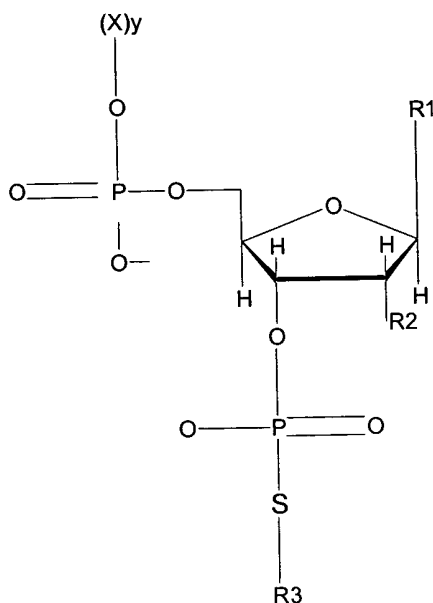
7. (Original) The method of claim 6, wherein said activator is iodonitrobenzene.

8. (Original) A method of molecular cloning comprising, contacting an insert comprising a polynucleotide-3' phosphorothiolate with an acceptor vector under conditions that allow formation of a phosphodiester bond between said insert and said acceptor vector to generate a vector comprising an insert polynucleotide.

9. (Original) The method of claim 8, further comprising transforming said vector comprising an insert polynucleotide into a host cell.

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10. (Amended) The method of claim 8, wherein said polynucleotide-3' phosphorothiolate ~~further comprises a 3' SNP moiety~~ comprises a moiety having the formula:



wherein,

X is a nucleotide;

y is a positive integer;

R1 is a nucleotide base;

R2 is a hydrogen atom or hydroxyl; and

R3 is nitrophenyl.

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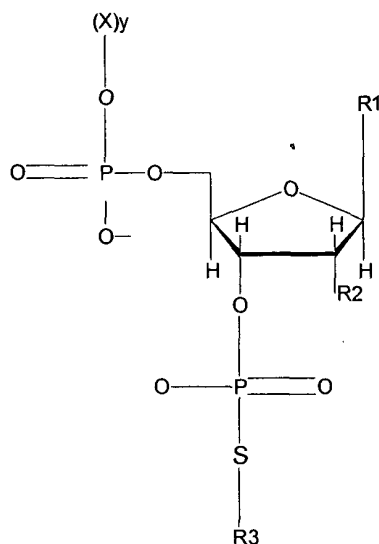
11. (Amended) ~~The method of claim 8, further comprising the step:~~ A method of molecular cloning comprising:  
    (a) contacting a polynucleotide-3' phosphorothiolate precursor and iodonitrobenzene under conditions sufficient to react said polynucleotide-3' phosphorothiolate precursor and said iodonitrobenzene to produce said a polynucleotide-3' phosphorothiolate, and  
    (b) contacting an insert comprising said polynucleotide-3' phosphorothiolate with an acceptor vector under conditions that allow formation of a phosphodiester bond between said insert and said acceptor vector to generate a vector comprising an insert polynucleotide.

12. (Original) A method of molecular cloning comprising, contacting a vector comprising a polynucleotide-3' phosphorothiolate with an acceptor polynucleotide, under conditions that allow formation of a phosphodiester bond between said vector and said acceptor polynucleotide to generate a vector comprising said acceptor polynucleotide.

13. (Original) The method of claim 12, further comprising transforming said vector comprising said acceptor polynucleotide into a host cell.

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14. (Amended) The method of claim 12, wherein said polynucleotide-3' phosphorothiolate ~~further comprises a 3' SNP moiety~~ comprises a moiety having the formula:



wherein,

X is a nucleotide;

y is a positive integer;

R1 is a nucleotide base;

R2 is a hydrogen atom or hydroxyl; and

R3 is nitrophenyl.

15. (Original) The method of claim 12, wherein said vector further comprises a 3' phosphorothiolate moiety at one or more terminal ends.

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16. (Amended) ~~The method of claim 12, further comprising the step:~~ A method of molecular cloning comprising:  
    (a) contacting a polynucleotide-3' phosphorothiolate precursor and an activator under conditions sufficient to react said polynucleotide-3' phosphorothiolate precursor and said activator to produce said a polynucleotide-3' phosphorothiolate, and  
    (b) contacting a vector comprising said polynucleotide-3' phosphorothiolate with an acceptor polynucleotide, under conditions that allow formation of a phosphodiester bond between said vector and said acceptor polynucleotide to generate a vector comprising said acceptor polynucleotide.

Claims 17-56 (Currently canceled)

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#### REMARKS

Claims 1-56 are pending in the present application, with claims 17-56 having been withdrawn from consideration. Claims 1, 3, 4, 7, 8, 10, 12, 14 and 15 have been deemed allowable in the Office Action mailed January 29, 2003. Claims 17-56 have been canceled herein without prejudice to Applicants' pursuing these claims in one or more related applications. Claims 2, 5, 6, 10, 11, 14 and 16 have been amended herein. Thus, claims 1-16 are presently under examination.

#### Regarding the amendments

Claims 2, 10 and 14 have been amended to replace the term "3' SNP moiety" with the chemical formula of a 3' SNP moiety. Support for these amendments can be found throughout the specification, for example, at page 17, lines 5-8, which indicates that a 3'-SNP is a "3'-phosphorothiolate moiety in which the sulfur molecule is bound to a nitrophenyl, that is when R3 = nitrophenyl." These amendments also are supported at page 9, line 27, to page 10, line 17, which indicates that a 3'-phosphorothiolate moiety is a nucleotide having at least one phosphate group linked by a phosphodiester bond at the 3' position of the sugar ring, the phosphate group having a phosphate oxygen substituted by sulfur. Thus, a 3' SNP moiety can be represented by the chemical formula for a polynucleotide-3' phosphorothiolate, as shown on page 10 of the specification, wherein  $y$  = a positive integer and R3 = nitrophenyl.



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Claim 5 has been amended to independent form. This amendment is supported in the specification, for example, at page 35, lines 11-22, which indicates that transformation of a ligated polynucleotide product (a "polynucleotide-3' phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide," as recited in claim 5) into a host cell is useful for generating a polynucleotide product; and in claims 1 and 5 as originally filed.

Claims 6, 11, and 16 have been amended to independent form. These amendments are supported, for example, by claims 1 and 6; claims 8 and 11; and claims 12 and 16, as originally filed, respectively.

As set forth above, the claim amendments do not add new matter. Therefore, Applicants respectfully request that the Examiner enter the amendments.

#### Regarding the drawings

The Office Action states that the drawings filed with the present application on June 15, 2001, are objected to by the Examiner. Applicants submit herewith copies of formal drawings corresponding to Figures 1-8 (Appendix A), which are being filed concurrently with the present response.

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Regarding the claim objection

The Office Action states that claim 2 is objected to because the term "SNP" is an abbreviation that can be used only after it appears once in a claim. Applicants have amended claim 2 herein to replace the objected term with a corresponding chemical formula. In view of this amendment to claim 2, Applicants request removal of this claim objection.

Regarding the indefiniteness rejections

The rejection of claims 5, 6, 9, 11, 13 and 16 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite are respectfully traversed. Applicants submit that claims 5, 6, 9, 11, 13 and 16 are clear and definite as written.

Claim 5 stands rejected as indefinite in view of the phrase "a polynucleotide-3'phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide" for allegedly lacking antecedent basis in claim 1. Applicants respectfully submit that the scope of claim 5 would be reasonable ascertainable by those skilled in the art because an outcome of practicing the method of claim 1 is generation of "a polynucleotide-3' phosphorothiolate having a phosphodiester bond with said acceptor polynucleotide." Nevertheless, Applicants have amended claim 5 to independent form.

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Claim 6 stands rejected as indefinite as allegedly lacking antecedent basis in claim 1. Applicants respectfully submit that because claim 6 introduces an additional step into claim 1, the claim 6 is anteceded by claim 1. Nevertheless, Applicants have amended claim 6 to independent form.

Claim 9 stands rejected as indefinite in view of the phrase "said vector comprising an insert polynucleotide" because it is allegedly unclear whether "an insert polynucleotide" in claim 9 is different from "an insert" in claim 9. Applicants respectfully point out that claim 8 recites a "vector comprising an insert polynucleotide" that is generated by contacting an insert comprising a polynucleotide-3' phosphorothiolate with an acceptor vector. Therefore, claim 8 provides antecedent basis for the phrase "said vector comprising an insert polynucleotide," as recited in claim 9.

Claim 11 stands rejected as indefinite for allegedly lacking antecedent basis in claim 8. Applicants respectfully submit that claim 11 introduces an additional step into claim 8, and therefore has antecedent basis in claim 8. Nevertheless, Applicants have amended claim 11 to independent form.

Claim 13 stands rejected as indefinite in view of the phrase "said vector comprising said acceptor polynucleotide" for allegedly lacking antecedent basis in claim 12. Applicants respectfully point out that claim 12 recites a "vector comprising an acceptor polynucleotide" that is generated by contacting a vector comprising a polynucleotide-3' phosphorothiolate with an

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acceptor polynucleotide. Therefore, claim 12 provides antecedent basis for the phrase "said vector comprising said acceptor polynucleotide," as recited in claim 13.

Claim 16 stands rejected as indefinite for lacking antecedent basis with respect to claim 12. Applicants respectfully submit that claim 16 introduces an additional step into claim 12, and therefore has antecedent basis in claim 12. Nevertheless, Applicants have amended claim 16 to independent form.

In view of the above amendments and remarks, Applicants respectfully request removal of the rejection of claims 5, 6, 9, 11, 13 and 16 under 35 U.S.C. § 112, second paragraph.

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CONCLUSION

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned agent or Cathryn Campbell.

Respectfully submitted,

July 23, 2003  
Date

Pamela M. Guy  
Pamela M. Guy  
Registration No. 51,228  
Telephone No. (858) 535-9001  
Facsimile No. (858) 535-8949

McDERMOTT, WILL & EMERY  
4370 La Jolla Village Drive,  
7<sup>th</sup> Floor  
San Diego, California 92122

In re Application of	)	Confirmation No: 7878
Burgin and Stewart	)	Group Art Unit: 1634
	)	Examiner: Lu, Frank Wei Min
Serial No: 09/882,274	)	
	)	
Filed: June 15, 2001	)	
	)	
For: USE OF	)	
PHOSPHOROTHIOLATE	)	
POLYNUCLEOTIDES IN	)	
LIGATING NUCLEIC ACIDS	)	
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#### **APPENDIX A**

Attached are  
Figures 1-8  
(pages 1-8)